

## REMARKS

The amendments to pages 40, 50 and 59 of the specification correct typographical errors. A marked up version of the amendments to the specification are attached hereto as **Exhibit A**. New claims 43-58 are supported throughout the specification. In particular, methods of detecting a cancerous cell with an EGFL6 specific antibody are supported at page 9, lines 24-28 and page 11, lines 2-4. Detection of EGFL6 in a biological sample, such as tissues, cells, blood, serum, lymphatic fluid, urine, cerebrospinal fluid, prostatic fluid and ascites fluid, is supported at page 10, line 25 through page 11, line 1, and page 90, line 1 through page 91, line 8. Labeled antibodies are supported at page 85, lines 12-17. Cancer in general is supported at pages 9-11, 65-66 and 107-109, including brain cancer (page 9, line 7-13, page 66, lines 20-22), prostate cancer (page 9, line 16-17, page 66, line 17, page 109, line 18-24), breast cancer (page 9, lines 18-19), skin cancer (page 66, lines 10-11), lymphoma (page 66, lines 10-11), sarcoma (page 69, lines 20 and 25), colon cancer (page 9, line 19, page 66, lines 15-16, page 109, line 18-24), leukemia (page 62, lines 8-16), ovarian cancer (page 66, lines 17-19), pancreatic cancer (page 16, line 15) and lung cancer (page 66, lines 12-13, page 109, lines 18-14). These amendments do not add new matter to the application.

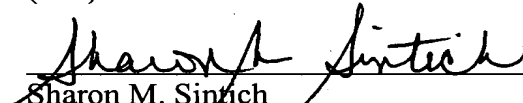
Claims 1-42 are canceled solely to reduce the filing fee. The Applicants do not intend by these or any other amendments to abandon the subject matter of any claim as originally filed, and reserve the right to pursue such subject matter in this application or related applications, including but not limited to parent applications and continuing applications.

The figures as filed were informal, therefore Substitute Formal Figures 1-5 (5 pages) are submitted herewith. The information depicted in the substitute drawing is identical to that in the drawing as originally filed and do not add new matter to the application.

Respectfully submitted,

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**EXHIBIT A**  
**MARKED UP VERSION OF AMENDED SPECIFICATION AND CLAIMS**

In the Specification

At page 40 line 17:

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, e.g., Invitrogen, San Diego, Calif., U.S.A. (the [MaxBat.RTM] MAXBAT™ kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucleotide of the present invention is "transformed."

At page 40 line 26:

The protein of the invention may be prepared by culturing transformed host cells under culture conditions suitable to express the recombinant protein. The resulting expressed protein may then be purified from such culture (i.e., from culture medium or cell extracts) using known purification processes, such as gel filtration and ion exchange chromatography. The purification of the protein may also include an affinity column containing agents which will bind to the protein; one or more column steps over such affinity resins as concanavalin A-agarose, [heparin-toyopearl.RTM] HEPARIN-TOYOPEARL™ or [Cibacrom blue 3GA Sepharose.RTM.] CIBACROM 3GA SEPHAROSE™; one or more steps involving hydrophobic interaction chromatography using such resins as phenyl ether, butyl ether, or propyl ether; or immunoaffinity chromatography.

At page 50 line 24:

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor

cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient mounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I [ .alpha.]  $\alpha$  chain protein and [ .beta..sub.2]  $\beta_2$  microglobulin protein or an MHC class II [ .alpha.]  $\alpha$  chain protein and an MHC class II [ .beta.]  $\beta$  chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

At page 59 line 21:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Marguiles, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28); Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25:1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153:1762-1768, 1994.